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RESEARCH ARTICLE

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Validation of an automatic software in assessing fetal brain volume from three dimensional ultrasonographic volumes: Comparison with manual analysis

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Abstract

Objective: This study was aimed to test the agreement between a manual and an automatic technique in measuring fetal brain volume (FBV) from three-dimensional (3D) fetal head datasets.

Methods: FBV were acquired independently by two operators from low risk singleton pregnancies at a gestational age between 19 and 34 weeks. FBV measurements were obtained using an automatic software (Smart ICV™) and manually by Virtual Organ Computer-aided AnaLysis (VOCAL™). Intraclass correlation coefficient (ICC) were calculated to assess reliability, while bias and agreement were evaluate by examining Bland–Altman plots. The time spent in measuring volumes was calculated and values obtained compared.

Results: Sixty-three volumes were considered for the study. In all the included volumes successful volume analysis were obtained with both techniques. Smart ICV™ showed a high intra-observer (0.996; 95% CI 0.994–0.998) and inter-observer (ICC 0.995; 95% CI 0.991–0.997). An excellent degree of reliability was found when the two techniques were compared (ICC 0.995; 95% CI 0.987–0.998). The time required to perform FBV was significantly lower for Smart ICV™ than VOCAL™ (8.2 ± 4.5 vs. 121.3 ± 19.0 s; $p < 0.0001$).

Conclusions: The measurement of FBV is feasible with both manual and automatic techniques. Smart ICV™ showed an excellent intra- and inter-observer reliability associated with a valuable agreement with volume measurements obtained manually with VOCAL™. Volumes may be measured significantly faster with smart ICV™ than manually and this automatic software has the potential to become the preferred methods for the assessment of FBV.

KEYWORDS
3D ultrasound, automatic software, brain volume, fetal CNS

1 | INTRODUCTION

The ultrasonographic measurement of fetal head circumference (HC) is the standard parameter used in establishing the brain growth.[1] However, HC only reflects the size of the head, including the skull, that may not reflect the real size of the brain since the spaces between the two structures may be increased in case of an abnormal growth of the central nervous system resulting in normal HC size despite the existence of a small brain.[2] Fetal brain volume (FBV) may be directly assessed by magnetic resonance (MR)[3,4] and there are evidences that it correlates with postnatal neurodevelopment better than HC size in different clinical scenarios such as in fetuses affected by congenital heart disease, infection and growth restriction.[2,5,6]

Despite MR is considered the gold standard for volume measurements, this technique is not routinely used in fetal imaging for its high cost and need of fetal quiescence. Consequently, it is actually used only as supplemental imaging tool in presence of abnormal ultrasonographic findings.[7]

Three-dimensional (3D) ultrasound has been applied for obtaining direct measurement of the placenta and fetal organ volumes.[8–10] This is generally obtained using Virtual Organ Computer-Aided-Analysis (VOCAL™) methodology, that allows volume calculation by sequentially rotating around a fixed axis the organ of interest through a number of steps. However, this technique is time consuming, requires a specific training of the operators and showed a low inter-observer reproducibility.[11]

Automatic computational-based methods may overcome these limitations and attempts were mainly done on hypoechogenic where the borders of the structure to analyze result well defined. To date this approach has been tested to the fetal heart chambers and other fetal fluid-filled organs.[11–13] More recently systems based on the analysis of big data and advanced pattern recognition algorithms has been developed to obtain automatic evaluation of solid structures.[14] Among these an automatic tool (Smart Intracranial Volume [Smart ICV™]) designed to evaluate FBV has become available.

The objectives of this investigation were: (1) to assess inter-, intra-observer and inter-method agreements for FBV measurement performed using Smart ICV™ and VOCAL™; (2) to evaluate differences in the time necessary by each method to obtain volume measurements.

2 | METHODS

2.1 | Population

This was a prospective cross-sectional observational study considering singleton pregnancies attending our unit for routine ultrasonographic examination at 19–34 weeks of gestation from 15 January to 15 April 2023. Criteria of inclusion was a confirmed gestational age as assessed by crown-rump length at the 11–14 weeks scan. We excluded fetuses with chromosomal, genetic, or structural anomalies detected ultrasonographically or mother with diseases present before pregnancy (pregestational diabetes, chronic hypertension, and immune diseases) or occurring during pregnancy (gestational diabetes, gestational hypertension, and preeclampsia). The research followed the principles of the Declaration of Helsinki for Medical Research involving Human Subjects and our Ethical Board approved the study protocol (RS 45.22; March 29, 2022). A signed informed consent was provided by all the included pregnancies.

2.2 | Ultrasound examination

All the ultrasonographic studies were obtained using Mindray Nuewa i9 (Mindray Medical, Shenzhen, China) using transabdominal volumetric probes.

All women underwent a detailed assessment of fetal anatomy and growth following Italian, ISUOG and AIUM guidelines.[15–17]

FBV were acquired following a technique previously reported,[18] starting with an axial plane of the fetal brain at the level of the transcerebellar view. The angle of insonation between the cerebral midline and the incident ultrasound beam was kept approximately at 45° in order to limit the acoustic shadow of the skull base on the brain structures of the reconstructed planes. The angle of sweep acquisition ranged from 45° to 60° according to gestational age to allow to include within the volume the full fetal head. Volumes were obtained waiting for fetal rest and during maternal apnea.

After volume acquisition of fetal head, the system could automatically display 3D image of intracranial tissue and calculate its volume using an automatic software (Smart ICV™ Mindray Medical, Shenzhen, China) (Figure 1; Video 1).

Evaluation of FBV volume was also measured manually using the VOCAL™ software included in the ultrasonographic equipment in 20 randomly selected volumes. This involved rotating the image around a reference axis at intervals of 30° and tracing the border of the fetal brain six times and the total FBV was then reconstructed automatically by computer.

2.3 | Study design and statistical analysis

In order to assess the intra-observer variability one of the Author (JLAL) acquired twice the fetal head volumes at the beginning and end of ultrasonographic sessions and smart ICV software was then applied on both datasets. To evaluate inter-observer variability a second sonographer (SR) blind of the measurements obtained by the first operator independently acquired on the same day a single brain volume and applied the automatic analysis. Measurements with VOCAL™ were performed at least at 2-week interval by JLAL. Volumes were analyzed in a random order from the acquisition and the operator was unaware of the results obtained in the automatic system.

Continuous variables were reported as mean and standard deviation or median and interquartile range according to their distribution, while categorical variables as number (n) and percentage (%).

To evaluate the intra- and inter observer agreement of smart ICV™ and reliability between the two techniques the interclass correlations coefficients (ICC) and their 95th confidence interval (95th CI) were calculated.

The intra-observer, inter-observer and inter-method agreements were all calculated using the proportionate Bland–Altman plots (difference in FBV divided by the mean of both measurements expressed as percent against the mean FBV of the two measurements).

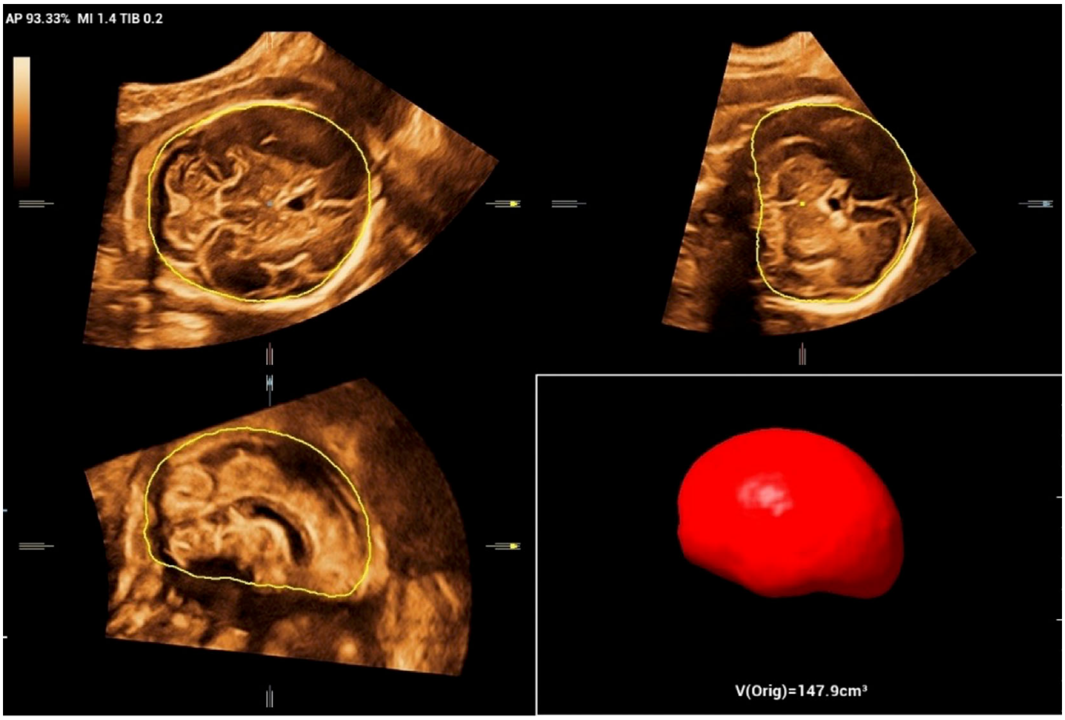

FIGURE 1 3D ultrasound image of fetal brain at 27 weeks of gestation and brain volume obtained with the automated software Smart ICV™.

TABLE 1 Characteristics of the pregnancies considered.

Variables	Median, *N*	IQR %
Maternal age (years)	34.5	31–37
Body mass index, BMI, kg/m^2	22.1	20.2–27.0
Nulliparae *n* %	33	52.4%
Caucasian ethnicity *n* %	63	100%
Male fetus *n* %	30	47.6%
Gestational age at ultrasonographic examination (weeks)	25	22–30

The time required to calculate FBV with the two methods was recorded and their values compared by Student's *t* test after controlling for their normal distribution.

MedCalc (MedCalc Software Ltd, Ostend, Belgium) and SPSS (SPSS, System for MacOS version 27, Chicago, IL) software were used for statistical analysis. A *p* value <0.05 was considered as statistically significant.

3 | RESULTS

A cohort of 68 women attending the antenatal clinic for ultrasonographic examination were included in the study. In five women it was not possible to record brain volume due poor imaging quality (*n* 3) and excessive fetal movements (*n* 2) leaving 63 volume datasets for the

TABLE 2 Intraclass correlation coefficient (ICC) and 95th confidence intervals (CI) obtained for intra-observer, inter-observer and inter-method fetal brain volume calculation.

	ICC	95% CI
Intra-observer	0.996	0.994–0.998
Inter-observer	0.995	0.991–0.997
Smart ICV™ versus VOCAL™	0.994	0.987–0.998

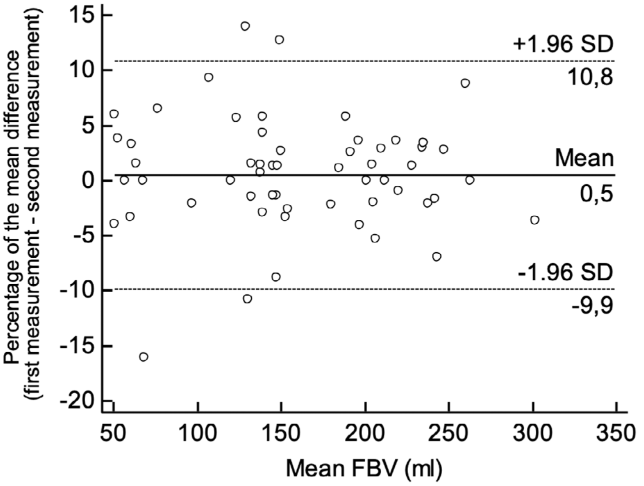

FIGURE 2 Bland–Altman plot for the percentage of the mean difference and 95% limits of agreement for intra-observer (A) and inter-observer (B) measurements performed by Smart IVC™.

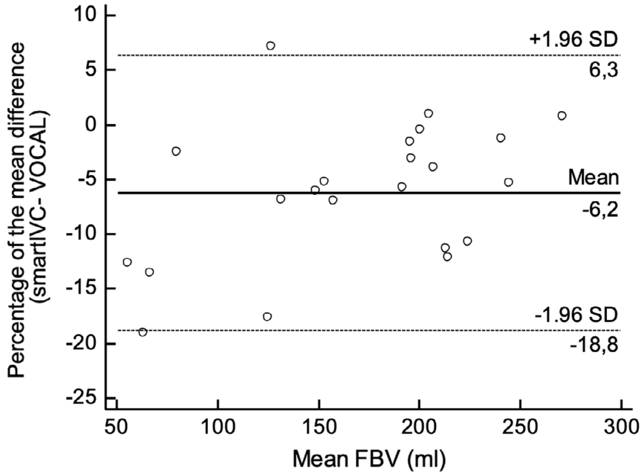

FIGURE 3 Bland–Altman plot for the percentage of the mean difference and 95% limits of agreement between for Virtual Organ Computer-aided AnaLysis (VOCAL™) and Smart IVC™ for fetal brain volume measurement.

analysis. In 50 of the 63 fetuses considered the fetal head volume was also acquired by the second operator. Their characteristics are reported in Table 1.

A high degree of reliability was observed for both the intra-observer (ICC 0.996) and inter-observer (0.995) volume measurements, as reported in Table 2. Figure 2 shows the Bland–Altman plot for the percentage % of the mean difference and its 95% limits of agreement for the intra-observe (mean 0.5%; 95% limits of agreement −9.8% to 10.8%) inter-observer measurements (mean −0.5%; 95% limits of agreement −10% to 10.1%).

Similarly a high degree of reliability for FBV was found between smart ICV and VOCAL™ (ICC 0.994) (Table 2). In Figure 3 the Bland–Altman plots are displayed for the percentage of the mean difference and 95% limits of agreement between smart ICV™ and VOCAL™ measurements. Volume measurements performed with VOCAL™ were slightly smaller than those performed with Smart ICV™ (mean −6.03%; 95% limits of agreement, −18.7% to 6.6%). The time required to measure FBV, starting from the upload of the volumes, was significantly shorter for Smart ICV™ than it was for VOCAL™ (8.2 ± 4.5 s vs. 121.3 ± 19.0 s; $t = 16.77$; $p < 0.0001$).

4 | DISCUSSION

4.1 | Main findings

The findings of this study show that FBV measurements using manual or automatic methods are feasible. Despite VOCAL™ had slightly lower measurements that Smart ICV™, the high inter-method ICC found suggest that both techniques may be used interchangeably.

Further Smart ICV™ showed an excellent degree of reliability, as demonstrated by the high intra- and inter-observers agreement and resulted significantly faster than VOCAL™.

4.2 | Strength and limitations

The principal strengths of the study are its prospective design, inclusion of unselected women undergoing routine second and third trimesters ultrasound and the presence of operators blind each other of FBV values. A limitation is that the lack of validation of the measurements performed for each method for the unfeasibility to calculate FBV in vivo. Besides, VOCAL™ has been extensively tested in different settings[8,10] and is considered the gold standard 3D method for performing volumetric assessment, against which Smart ICV™ was tested. A second limitation of our study is represented by the fact that fetal head volumes were acquired by sonographers with experience in 3D ultrasound and our experimental design does not allow to exclude that the same performance of Smart ICV™ may be achieved with operators with a different degree of training.

4.3 | Comparison with existing literature

In the past few years several studies have attempted to study FBV using MR or ultrasound showing a marked inconsistency in the results obtained. This may be due by the different measurements technique applied during RM or operator dependency by 3D ultrasound.[2,3] Irrespectively of these findings FBV resulted an important imaging biomarker of neurodevelopment after birth. Indeed, in fetuses with a structural cardiac anomaly, a small FBV resulted a strong and independent predictor of 2-year neurodevelopment at 2 years.[5] Further in fetuses exposed to maternal alcohol intake or Zika infection there are evidences of a selective reduction of FBV that correlates with their neurological outcome.[19,20] Similarly in growth restricted fetuses FBV may be affected and these modifications persist at 10 years of age.[21,22]

These findings highlight the importance of evaluating FBV together with other neuroimaging markers during prenatal life in the attempt of identify fetuses at risk of abnormal neurodevelopment outcome.[23] The application of an automatic system based on ultrasonographic examination s may overcome the difficulties present in MR and manual 3D reconstruction may make simpler the volumetric analysis of fetal brain opening the potential of its application in research frameworks.

5 | CONCLUSIONS

The application of Smart ICV™ software enables to obtain the fully automated assessment of the FBV. The findings from this study demonstrate its applicability during second and third trimesters ultrasonographic examination reaching an excellent intra- and inter-observer agreement and reliability with manual technique and requiring rapid time of acquisition compatible with clinical practice. Further studies assessing the role of FBV in the prenatal detection of abnormalities of central nervous system development are needed to assess its potential usefulness in the daily clinical practice.

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CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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